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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,386	02/28/2005	Leonard Mackles	CHAV3.0-032PCT/US	3839

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EXAMINER	
COTTON, ABIGAIL MANDA	
ART UNIT	**PAPER NUMBER**
1617	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,386	MACKLES, LEONARD	
	Examiner	Art Unit	
	Abigail M. Cotton	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the amendment and remarks submitted on March 16, 2007. Claims 25-43 are pending in the application and are being examined on the merits herein.

The rejection of claim 28 under 35 U.S.C. 112, first paragraph, as containing impermissible new matter, is withdrawn in view of Applicant's amendment to the claim. The objection to the specification is also being withdrawn in view of Applicant's amendment to page 4 line 8 of the specification to correct the minor typo-type error.

The provisional obviousness-type double patenting rejection made over U.S. Patent Application Serial No. 10/406,869 is being withdrawn in view of the abandonment of that application.

Applicant's arguments regarding the rejections of the claims over the prior art have been fully considered but they are not persuasive.

The claims remain rejected as follows.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 25-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over DE 199 25 289 A1 to Klocker et al, published December 7, 2000, in view of U.S. Patent No. 5,897,858 to Haslwanter et al, issued April 27, 1999, and further in view of JP 07-076526 to Omori et al, published March 20, 1995.

Klocker et al. teaches a pharmaceutical composition for the nasal administration of a water-soluble active agent, comprising the active agent, a neutral oil and optionally a solubility enhancer (see abstract, in particular.) Klocker et al. teaches that the composition is free of water (non-aqueous), and does not require propellants or preservatives (see abstract and column 2, lines 9-15, in particular.) Klocker et al. teaches that the oil can be a triglyceride, such as triglycerides having a fatty acid content that includes caproic and caprylic acid (see paragraph bridging columns 2-3, in particular.) Klocker et al. teaches that the composition can be administered via sprays and/or nose drops (see column 2, lines 20-25, in particular.)

Accordingly, it is considered that Klocker et al. teaches providing a liquid spray for administration of a bioactive material to the nasal cavity having a pharmacologically acceptable non aqueous liquid carrier that is a triglyceride, as in part (a) of claim 25, and a pharmacologically acceptable water soluble bio-active material, as in part (b), the spray being non-aqueous. Regarding the recitation that the bioactive material is soluble in the glycol but insoluble in the carrier, the Examiner notes that Klocker et al. teaches the same carrier as that recited, namely a triglyceride, and teaches that the bio-active material is water-soluble, and thus it follows that the bio-active material is insoluble in non-aqueous materials, such as the triglyceride oil, and is soluble in other water-soluble substances, such as the glycol. It is noted that the solubility of compound is a property thereof, and a product and its properties are inseparable. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)

Klocker et al. does not specifically teach that the composition contains an acceptable water soluble glycol, or an ester of a water soluble acid, as recited in claim 25. However, Klocker et al. does teach that the composition can have other components that improve uptake of the drug through the mucous membranes of the nose (see column 5, lines5-22, in particular.)

Haslwanter et al. teaches a nasal spray having polyethylene glycol (see abstract, in particular.) Haslwanter teaches that water soluble polyethylene polymers can be used to promote moisturization of the nasal spray composition in the nasal cavity (see

column 3, lines 55-58, in particular), and teaches that other such moisturization agents include propylene glycol and glycerin (see column 4, lines 24-35, in particular.) Regarding the recitation that the glycol is soluble in the ester of the water soluble acid, it is noted that as Haslwanter et al. teaches the same glycols as that being claimed, it follows that the glycols are also soluble in the claimed ester. It is noted that the solubility of compound is a property thereof, and a product and its properties are inseparable. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963). Thus, Haslwanter et al. teaches that pharmacologically acceptable water soluble glycols can be provided in nasal spray compositions to moisturize the nasal cavity, and thus teaches providing part (c) of claim 25.

Accordingly, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to provide the water soluble glycol of Haslwanter et al. in the nasal spray composition of Klocker et al, because Klocker et al. teaches a composition that can be applied nasally that and can have other components that improve uptake of the drug through the mucous membranes of the nose, whereas Haslwanter et al. teaches water soluble glycols for nasal sprays that improve moisturization of the nasal cavity, and thus improve administration of the drugs. Thus, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to provide the water soluble glycols of Haslwanter et al. in the nasal spray compositions of Klocker et al, with the expectation of providing an

ingredient suitable for improving the administration of the drug by moisturizing the nasal cavity.

Regarding the amount of the water-soluble glycol provided in the composition, as recited in part (c) of claim 25, it is noted that Haslwanter et al. teaches that an amount of polyethylene glycol provided can be 2.5-10% weight/volume, and other moisturizers can be provided in an amount of 1-10% by weight (see abstract, in particular), which ranges meet and/or overlap with the recitation that the glycol comprises from 1 to about 5% by weight of the total composition. Furthermore, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of the glycol provided in the composition, according to the guidance provided by Klocker et al. and Haslwanter et al, to provide a composition having desired properties. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Klocker et al. and Haslwanter et al. do not specifically teach combining a water insoluble ester of a water soluble acid into the composition, as recited in part (b) of claim 25, such as a lactate ester, as in claim 33, including cetyl, lauryl and isostearyl lactate esters, as in claim 35. However, as discussed above, Klocker et al. does teach

that the composition can have other components that improve uptake of the drug through the mucous membranes of the nose (see column 5, lines5-22, in particular.)

Omori et al. teaches a transcutaneous absorption preparation containing lactic acid esters that improve the absorption and penetration of drugs through the skin (see abstract, in particular.) Omori et al. teaches that that lactate esters can be formed with fatty alcohols with carbon numbers of 12-18, include cetyl lactate and lauryl lactate (see paragraph 0007, in particular.) Omori et al. teaches that for mucosal skin surfaces in particular, the lactic acid ester penetration enhancer allows easy absorption without excessive stimulation of the mucosal surface (see paragraph 0019, in particular.) Regarding the recitation that the ester is an insoluble ester of a water soluble acid that is soluble in the carrier, it is noted that as Omori et al. teaches the same lactic acid esters as that being claimed, it follows that the esters also have the same solubility characteristics. It is noted that the solubility of compound is a property thereof, and a product and its properties are inseparable. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963). Thus, Omori et al. teaches that the esters as in part (b) can be provided to enhance penetration of drugs across mucous membranes.

Accordingly, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to provide the penetration enhancing lactic acid esters of Omori et al. in the nasal spray composition of Klocker et al, because Klocker et al. teaches a composition that can be applied nasally that and can have other

components that improve uptake of the drug through the mucous membranes of the nose, whereas Omori et al. teaches that the lactic acid esters enhance penetration of drugs through mucous membranes without excessive stimulation of the membranes. Thus, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to provide the lactic acid esters in the nasal spray compositions of Klocker et al, with the expectation of providing a composition having improved permeation of the drug through the nasal mucous membranes.

The references do not teach the specific steps of dissolving the bioactive material in a glycol, then dissolving in the ester, and dissolving in the carrier, as recited in claim 25. However, as Klocker et al, Haslwanter et al. and Omori et al. teach the desirability of providing the each of the components (a)-(d) in the nasal spray composition, it is considered that one of ordinary skill in the art would have found it obvious to combine vary and/or optimize the steps by which the components are added together, with the expectation of achieving a product suitable for nasal administration. It has been held that merely changing the order of steps in a multi-step process is not a patentable modification absent a showing of unexpected results. *Ex parte Rubin* 128 USPQ 440 (POBA 1959.)

It is furthermore noted that, for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, the transitional phrase "consisting essentially of" is being construed as equivalent to "comprising," absent a clear indication in the

specification or claims of what is meant by, i.e. what is being excluded from the method and/or composition, by the phrase "consisting essentially of." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355, and MPEP 2111.03.

Regarding claim 26, Klocker et al. teaches that the oil can have medium chain triglycerides (see column 2, lines 65-68, in particular.) Regarding claims 27-28, Klocker et al. teaches that a preferred oil is Miglyol 810, which has capric and caprylic fatty acids chains esterified with glycerin or propylene glycol, and also teaches that such oils can be obtained via esterification of such fatty acids as caproic acid (see paragraph bridging column 2 through 3, in particular.) Thus, Klocker et al. teaches the carrier comprising a medium chain length propylene triglyceride, and teaches that the glyceride moieties can be selected from caprylic and caproic glycerides, as recited in the claims.

It is respectfully pointed out that instant claims 29-39 are product-by-process claims. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed Cir. 1985). See MPEP 2113. In the instant case, the combination of references render obvious providing a composition

for nasal administration that is non-aqueous and that has the components (a)-(d) as recited in claim 29.

Regarding the specific amount of each component, as in claims 29-30, it is noted that Klocker et al. teaches that the amount of active agent can be from 0.01-15% by weight (see column 4, lines 67-68, in particular), which overlaps with the amount recited in the claim, and exemplifies composition having an active agent (polyhexanide) in a Miglyol 840 oil in a 20% by weight formulation, which would result in about 80% by weight of the oil (see Example 4, in particular.) Haslwanter et al. teaches that the glycols can be provided in an amount of 2.5-10% weight/volume (polyethylene glycol) and 1-10% by weight/volume (e.g. propylene glycol (see abstract, in particular.) Omori et al. teaches that the lactic acid ester penetration enhancers can be provided in an amount of 1-30% by weight (see paragraph 0008, in particular.) Furthermore, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of each of the components provided in the composition, according to the guidance provided by Klocker et al, Haslwanter et al. and Omori et al, to provide a composition having desired properties, such as desired nasal administration properties. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.)

Regarding claims 31-32, Haslwanter et al. teaches providing polyethylene glycol and propylene glycol as moisturizing agents in the compositions, as discussed above. Regarding claims 33-35, Omori et al. teaches providing the alkyl lactates, including lauryl and cetyl lactate, as recited in the claims.

Regarding claim 40, Klocker et al. teaches that the composition can be administered by spraying into the nasal cavity (see column 2, lines 19-25, in particular.) It is furthermore noted that, for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, the transitional phrase "consisting essentially of" is being construed as equivalent to "comprising," absent a clear indication in the specification or claims of what is meant by, i.e. what is being excluded from the method and/or composition, by the phrase "consisting essentially of." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355, and MPEP 2111.03.

Regarding claims 36-39 and 41-43, Klocker et al. teach that the active agents administered by the composition drugs such as ephedrine and phenylephrine hydrochloride (see column 3, line 45 and 57, in particular), and thus teaches providing the decongestants as recited in the claim, a well as pharmaceutically acceptable salts thereof. It is furthermore noted that Klocker et al. teaches that the active agents are water soluble (see abstract, in particular), as discussed above, and thus it is considered that the drugs are in water-soluble form, as recited in claims 39 and 43.

Response to Arguments

Applicant's arguments filed March 16, 2007 have been fully considered but they are not persuasive.

In particular, Applicant argues that the references do not teach or suggest the specific order or steps of preparing the composition, as recited in the claims. Applicant argues in the remarks filed March 16, 2007, as well as the preliminary amendment filed on November 28, 2006, that it has been discovered that stable nonaqueous solution of the water soluble active can be prepared by dissolving the bioactive in a water soluble glycol, dissolving this mixture in an ester of a water soluble acid, and then combining the mixture into a nonaqueous liquid carrier that is a diglyceride, triglyceride or a mixture thereof. Applicant argues that the claimed method steps are not taught or suggested by the prior art and represent an improvement over the teachings of prior art such as Klocker et al, because according to Applicant, the prior art methods such as those of Klocker are not capable of solubilizing the active in the carrier.

The Examiner notes that, as discussed above, the combination of Klocker et al, Haslwanter et al. and Omori et al. render obvious an anhydrous liquid spray composition containing the claimed carrier, ester, water soluble glycol and water soluble bio-active material, as recited in claim 25. While the references do not specifically teach the steps of adding the bio-active material to the glycol, then adding to the ester, before

combining into the carrier, as claimed, it has been held that merely changing the order of steps in a multi-step process is not a patentable modification absent a showing of unexpected results. *Ex parte Rubin* 128 USPQ 440 (POBA 1959.) In the instant case, Applicant has not shown any evidence or other proof that changing the order of steps would result in a materially different product or that the instantly claimed order of steps otherwise gives unexpected results in the preparation of the spray formulation over other means of preparation. Accordingly, the instantly claimed method is deemed obvious over the teachings of Klocker et al, Haslwanter et al. and Omori et al.

Applicant further argues that Klocker et al. teaches only suspensions, and not solutions as claimed, and asserts that Klocker et al. merely engages in "some wishful disclosure" with regards to forming solutions of the active agents. The Examiner respectfully disagrees with this interpretation. It is noted that Klocker et al. teaches that the water soluble agents can be combined into the composition in the form of either a solution or a suspension (page 2 of English translation, in particular), and further teaches providing dissolving intermediaries in the composition that support and enable a solution of the water soluble active agent in the oil (see page 12 of English, translation, in particular), and thus it is considered that Klocker et al. clearly teaches forming solutions of the water soluble agents in the oil composition. Furthermore, as discussed above, as the combined references render obvious providing a composition with the same oil, ester, glycol and bio-active agent as claimed, it is considered that the

composition would necessarily also be in the form of a solution having the bioactive dissolved therein, as a product and its properties are inseparable.

Applicant also argues that the solvating agents such as those listed by Klocker et al. do not provide the desired solutions, as Applicant has tried to use such solvating agents without success. It should be noted that a showing of unexpected results, such as the ability of a method to dissolve actives where prior methods failed, must be based on evidence, not argument or speculation. In re Mayne, 104 F.3d 1339, 1343-44, 41 USPQ2d 1451, 1455-56 (Fed. Cir. 1997).

Applicant further argue that the Haslwanter et al. reference is not properly citable because it relates to aqueous nasal sprays, as opposed to anhydrous nasal sprays, and thus Applicant asserts the Haslwanter et al. reference is non related art. The Examiner respectfully disagrees. The Haslwanter et al. reference is directed to the teaching of nasal sprays, as is Klocker et al and the claimed methods, and teaches that the claimed glycols can be advantageously provided in such nasal sprays to moisturize the nasal cavity. Accordingly, as Haslwanter et al. is directed towards the development of nasal sprays and ingredients suitable for use therein, it is considered that Haslwanter et al. is analogous art with respect to the claimed method as well as Klocker et al.

Applicants also argue that the moisturization effect of the glycol as taught by Haslwanter et al. is irrelevant, and that "its importance lies in its unsuggested function

as a primary solvent in a three solvent chain" (see page 7 of Remarks filed on March 16, 2007.) The Examiner notes that the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Regarding the teachings of the lactate esters of Omori et al, Applicant argues that this teaching "has nothing to do with their use in the solution sequence which is the basis of the present invention," and notes that the criticality of the order of addition as recited in the claims has been shown in Example 1 of Applicant's specification. The reasons for combination of the lactate esters of Omori et al. with the composition of Klocker et al. and Haslwanter et al. have been discussed above, and lie in the fact that Omori et al. teaches that the lactate esters are capable of enhancing the penetration of drugs through mucous membranes, as is desired in nasal administration means. Regarding the asserted showing of criticality of the claimed method steps, the Examiner notes that Example 1 of the Applicant's specification provides an example of a suitable method of making the nasal compositions, which corresponds to the steps as claimed. However, Applicant has not provided any comparative examples or other studies to show that the sequence of method steps are indeed "critical" for forming the desired composition.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abigail M. Cotton whose telephone number is (571) 272-8779. The examiner can normally be reached on 9:30-6:00, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AMC

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